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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,423	03/01/2004	Pascal J. Goldschmidt-Clermont	1579-890	4961

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	
MAIL DATE	**DELIVERY MODE**
07/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/788,423	GOLDSCHMIDT-CLERMONT ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *3,5,7,9 and 14-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,8 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and remarks filed 5/7/07 are acknowledged. Claim 1 has been amended. Claims 1-26 are pending, however, claims 3, 5, 7, 9 14-26 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim.

Claims 1, 2, 4, 6, 8, 10-13 are under current examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 6, 8, 10-12 are rejected under 35 U.S.C. 103(a) as being obvious over *Linton et al* (Science 1995;267:1034-7), and as evidenced by *Reyes et al* (J Clin Med 2002;109:337-46).

Linton et al teach intravenous administering (BMT, mid-column, page 1037) normal (heterologous) bone marrow cells to ApoE-deficient mice (an art-recognized animal model for atherosclerotic disease) significantly reduced serum cholesterol levels of ApoE-/- mice. Two months after BMT, BMT recipient mice were challenged with high-fat diet for three months. Upon conduction of quantitative analysis of aortic atherosclerosis, *Linton et al* reported dramatic reduction of atherosclerotic lesion in normal BMT recipient mice compared to apoE-/- BMT recipient mice (e.g. page 1036). *Linton et al* concluded that transplantation of normal bone marrow into ApoE-/- mice results in correction of hypercholeserolemia and prevention of aortic and coronary atherosclerosis. Although not relied upon, it was well known in the art bone marrow cells contain endothelial progenitor cells that mature into vascular endothelial cells as taught by *Reyes et al*. The teaching of *Linton et al* differ from instant claims in that the stem cells were administered to an animal model for atherosclerotic disease, not a human patient. However, it was clear from reading the publication that the animal study was a feasibility study for treating the disease in humans.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method taught by *Linton et al* in a human subject with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the ultimate goal for conducting the animal study is to search for a cure of the disease in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1, 2, 4, 6, 8, 10, 11 are rejected under 35 U.S.C. 103(a) as being obvious over *Ishimori et al* (J Leuk Biol 2001;69:732-40).

Ishimori et al teach administering a mixture of normal heterolgous bone marrow cells (SJL/J) to ApoE-deficient mice with hypercholesterolemia and preexisting atherosclerotic lesions. *Ishimori et al* reported significant reduction of the cholesterol level and significant lesion regression of the atherosclerosis (e.g. the abstract, fig.4, and table 1). *Ishimori et al* concluded the resistance of SJL to atherosclerosis resides in the bone marrow-derived cells (e.g. page 738). The teaching of *Ishimori et al* differ from instant claims in that the stem cells were administered to an animal model for atherosclerotic disease, not a human patient. However, it was clear from reading the publication that the animal study was a feasibility study for treating the disease in humans.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method taught by *Ishimori et al* in a human subject with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the ultimate goal for conducting the animal study is to search for a cure of the disease in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1, 2, 4, 6, 8, 10, 11 are rejected under 35 U.S.C. 103(a) as being obvious over *Sakai et al* (Atherosclerosis 2002;161:27-34).

Sakai et al teach intravenously administering a mixture of normal heterolgous bone marrow cells with Apo-E deficient bone marrow cells (chimerism) to ApoE-deficient mice as a stem cell gene therapy strategy, and tested minimal requirement for the proportion of normal bone marrow. *Sakai et al* teach that 10% chimerism could significantly reduce the severity of the atherosclerosis (e.g. the abstract, fig.4, and § 3.3), wherein bone marrow cells contain endothelial progenitor cells that mature into vascular endothelial cells. The teaching of *Sakai et al* differ from instant claims in that the stem cells were administered to an animal model for atherosclerotic disease, not a human patient. However, it was clear from reading the publication that the animal study was a feasibility study for treating the disease in humans.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method taught by *Sakai et al* in a human subject with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the ultimate goal for conducting the animal study is to search for a cure of the disease in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1, 2, 4, 6, 8, 10, 11 are rejected under 35 U.S.C. 103(a) as being obvious *Rauscher et al* (AHA 2002 November, IDS).

Rauscher et al teach intravenous administering heterologous unfractionated bone marrow cells to ApoE-deficient mice and significantly reduce the atherosclerotic lesions throughout the arterial tree. The teaching of *Rauscher et al* differ from instant claims in that the stem cells were administered to an animal model for atherosclerotic disease, not a human patient. However, it was clear from reading the publication that the animal study was a feasibility study for treating the disease in humans.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method taught by *Rauscher et al* in a human subject with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the ultimate goal for conducting the animal study is to search for a cure of the disease in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1, 2, 4, 6, 8, 10-13 are rejected under 35 U.S.C. 103 (a) as being obvious over *Werner et al* (Arterioscler Thromb Vasc Biol 2002;22:1567-72).

Werner et al teach vascular injury induced atherosclerosis and treatment strategy using a carotid injury model. Gene marked bone marrow cells were administered six months prior to injury (prophylactic), and 10 days before the vascular injury (column 1, page 1568), the mice received daily doses of rosuvastatin (a proteinceous or non-proteinceous anti-atherosclerotic agent). *Werner et al* reported bone marrow cells are found predominantly at the endothelial monolayer (fig. 2c), and treatment with

rosuvastatin enhanced the circulating pool of endothelial progenitor cells and accelerated bone marrow-dependent reendohelialization of injured vascular wall in atherosclerosis (e.g. pages 1569-70, and fig. 4). The teaching of *Werner et al* differ from instant claims in that the stem cells were administered to an animal model for atherosclerotic disease, not a human patient. However, it was clear from reading the publication that the animal study was a feasibility study for treating the disease in humans.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method taught by *Werner et al* in a human subject with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the ultimate goal for conducting the animal study is to search for a cure of the disease in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on 571-272-0739. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
July 9, 2007